

Surgical Resection of Pulmonary Metastases From Gastric Cancer

YUKIHIDE KANEMITSU, MD, HARUHIKO KONDO, MD,* HITOSHI KATAI, MD,
HARUHIKO NAKAYAMA, MD, HISAO ASAMURA, MD, RYOSUKE TSUCHIYA, MD, AND
TSUGUO NARUKE, MD

Department of Surgical Oncology, National Cancer Center Hospital, Tokyo, Japan

Background and Objectives: There are no reports concerning surgical treatment on pulmonary metastases from gastric cancer. The aims of this study were to characterize patients with pulmonary metastasis from gastric cancer and to determine the efficacy of surgical therapy.

Methods: Between 1977 and 1993, 3,076 patients underwent curative resection for gastric cancer. Among them, four patients (0.1%) with pulmonary metastases from gastric cancer underwent pulmonary resection.

Results: All four patients had advanced gastric cancers involving regional lymph nodes far from the primary gastric lesion. The median tumor-free interval after the initial gastrectomy was 32.0 months (range: 19–48 months). All patients underwent a lobectomy for a solitary pulmonary lesion. Although transthoracic fine-needle aspiration cytology revealed adenocarcinoma in all cases, none of them were definitely diagnosed as metastasis from gastric cancer preoperatively. The diagnosis was obtained after pulmonary resection. All patients received postoperative chemotherapy or radiotherapy, or both. However, they all subsequently developed systematic metastases. The time interval to recurrence after pulmonary resection ranged from 6 to 36 months and they were all dead at a median follow-up of 24.3 months after the pulmonary resection.

Conclusions: An aggressive surgical approach was not warranted in patients with isolated resectable pulmonary metastases from gastric cancer. However, the possibility of surgical treatment could not be eliminated because surgery is the only diagnostic method for a solitary pulmonary nodule when there is some doubt about the diagnosis of primary or secondary lung cancer in patients with gastric cancer.

J. Surg. Oncol. 1998;69:147–150. © 1998 Wiley-Liss, Inc.

KEY WORDS: surgical resection; pulmonary metastasis; gastric cancer

INTRODUCTION

Many studies have demonstrated the significance of pulmonary resection for metastatic tumors from colorectal cancer or renal cell cancer [1–3]. However, no report concerning pulmonary resection for metastasis from gastric cancer has appeared in the literature. We had the opportunity to treat 4 of the 3,076 patients who underwent gastrectomy for gastric cancer in the National Cancer Center Hospital in Tokyo between 1977 and 1993 for pulmonary metastases. We have characterized these four patients and evaluated the outcome of surgical therapy.

MATERIAL AND METHODS

From 1977 through 1993, 3,076 patients in our institute were operated on with curative intent for gastric cancer microscopically proven to be adenocarcinoma. Vital statistics of all were obtained from the city registry

*Correspondence to: Haruhiko Kondo, MD, Division of Thoracic Surgery, National Cancer Center Hospital, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan. Fax No.: (81)3-3542-3815.
E-mail: hrkondoh@gan2.ncc.go.jp

Accepted 14 September 1998

TABLE I. Frequency and Mode of Hematogenous Recurrence of Gastric Cancer in 3,076 Patients

	Number of patients	Percentage	
Hematogenous recurrence	71	100.0 ^a	2.3 ^b
Lung and other organ metastases	15	21.1	0.5
Lung metastasis only	7	9.9	0.2
Multiple lesions	3	4.2	0.1
Solitary lesion	4 ^c	5.6	0.1
Other organ metastases	49	69.0	1.6

^aThe percentages for hematogenous recurrence at different sites out of a total of 71 recurrences.

^bThe percentage of patients with hematogenous recurrence out of the total number of 3,076 patients with gastric cancer.

^cResected cases for pulmonary metastatic lesions.

office and follow-up records. The most recent follow-up was in December 1997. In 71 (2.3%) of the 3,076 patients, hematogenous recurrence of cancer was confirmed by clinical or operative examination. Of the modes of hematogenous recurrence, metastasis to the mediastinum or pleura was not included in this study. Also excluded were the patients having multiple primary malignancies during the trace and those in whom pulmonary lesions were not correctly identified as to whether they were primary lung or secondary gastric cancer microscopically.

RESULTS

Table I summarizes the incidence and mode of hematogenous recurrence in the 3,076 patients. Of the 71 patients with hematogenous recurrence, 22 (31.0%) had lung metastasis. Of them, seven (31.8%) had metastases only in the lung. Four (57.1%) of these seven had solitary pulmonary metastases that were resected.

The clinicopathological features of the primary gastric cancer of the four patients who underwent resection for pulmonary metastases are shown in Table II. All were males, and the mean age at gastrectomy was 63.0 ± 7.3 years. There were three patients with Borrmann type II and one with superficial type. Three underwent total gastrectomies and another underwent partial gastrectomy. All gastrectomies were curative with tumor-free surgical margins and no residual tumor. Histological examination of the resected specimens revealed that all tumors were composed of differentiated adenocarcinoma and involved the muscularis propria or deeper. All patients had regional lymph node metastasis, which was the second level (N2 [4]), i.e., the main artery of the celiac trunk, the splenic hilus, or the pancreatic tail. No patient had received any treatment before gastrectomy. Patient 1 received postoperative adjuvant chemotherapy with 600 mg of tegafur orally each day for 22 months and patient 3 was administered UFT (tegafur and uracil) 400 mg/day orally for 32 months and mitomycin C at 0.2 mg/kg intravenously every 4 weeks for 6 months.

All of the pulmonary metastases were found during the outpatient follow-up examinations. Their clinical details are shown in Table III. The earliest pulmonary metastasis was detected 19 months after the gastrectomy in patient 4. The median tumor-free interval after gastrectomy was 32 months. All the pulmonary tumors were solitary nodules according to X-rays and CT. Although fine-needle aspiration cytology revealed adenocarcinoma, there was no definite diagnosis of pulmonary metastasis from gastric cancer in any cases. The tumor in patient 2 was resected as primary lung cancer. In the other three cases the tumors were resected to distinguish primary lung cancer from pulmonary metastasis. All resected specimens were diagnosed as pulmonary metastases from gastric cancer by histological examination, including immunohistochemistry. During a median follow-up of 14.2 months after the pulmonary resection, all patients had recurrence: three in the lung, three in the bone, one in the brain, one in the liver, and one in Virchow lymph node. All patients except patient 2 developed recurrence within 1 year after the pulmonary resection. Patients 1 and 3 received postoperative radiotherapy (60 Gy) as palliation for brain or bone metastases. Two patients received adjuvant chemotherapy, consisting of mitomycin C for patient 2 and cisplatin and 5-fluorouracil for patient 4. However, all patients died of metastatic tumors during a median follow-up period of 24.3 months after the pulmonary resection.

DISCUSSION

In recent years, advances in anesthesia and thoracotomy procedures have eliminated contraindications even for simultaneous bilateral pulmonary resections [5]. Modifications have led to more extensive use of resection, and to date there have been numerous reports of surgical treatment of metastatic pulmonary cancer [1–3,6,7]. At our facility, we have actively pursued surgical treatment for metastatic pulmonary cancer under the following criteria: first, there are no metastatic foci outside the lungs; second, the patient will tolerate the pulmonary resection and have a prospect of a good postoperative quality of life; third, the primary focus is controlled; and fourth, complete resection of the pulmonary metastatic focus is anticipated.

In our experience with 624 resections of metastatic pulmonary cancer from 1962 to 1995, the total 5-year survival rate of 37.7% (data not shown) shows little difference from that reported by Thomford et al. [6]. However, in compiling various cases, we encountered tumors offering a relatively good prognosis despite multiple metastases [2,3,7] like that from colorectal cancer, renal cell cancer, osteogenic or soft-tissue sarcoma, and, conversely, cancers with a poor prognosis despite what initially appeared to be a favorable set of circumstances. We

TABLE II. Clinicopathological Features of the Primary Gastric Cancer in Patients Who Underwent Pulmonary Resection*

Patient	Age (years)	Sex	Tumor site	Borrmann type	Depth of invasion	Histology	Gastrectomy	Lymphatic invasion	Venous invasion	Lymph node metastasis	pTNM
1	63	Male	P	II	ss	Differentiated adenocarcinoma	Total	+	+	+	pT2N2M0
2	53	Male	M	II	s	Differentiated adenocarcinoma	Total	—	+	+	pT3N2M0
3	66	Male	D	II	s	Differentiated adenocarcinoma	Partial	+	—	+	pT3N2M0
4	70	Male	M	Unclassified ^a	mp	Differentiated adenocarcinoma	Total	—	—	+	pT2N2M0

*P = proximal third of stomach; M = middle third of stomach; D = distal third of stomach; ss = subserosa; s = serosa; mp = muscularis propria.

^aSuperficial type.

TABLE III. Clinical Data of the Patients Who Underwent Pulmonary Resection for Metastases From Gastric Cancer: Details of the Pulmonary Metastases

Patient	Disease-free interval (month)	Number of metastases	Extrapulmonary metastasis	Type of resection	Time interval to recurrence (month)	Pattern of recurrence	Adjuvant therapy	Outcome after pulmonary resection
1	22	1	—	Lobectomy	8	Bone, brain	Radiotherapy	Dead at 23 months
2	39	1	—	Lobectomy	36	Lung, Virchow lymph node	Chemotherapy	Dead at 45 months
3	48	1	—	Lobectomy	6	Lung, liver, bone	Radiotherapy	Dead at 10 months
4	19	1	—	Lobectomy	9	Lung, bone	Chemotherapy	Dead at 19 months

now need to refine the indications applicable to each primary cancer.

In histological examination of autopsy cases, a 22.4%–52.3% incidence of pulmonary metastasis from gastric cancer has been reported [8,9]. While this is by no means infrequent, especially few cases of pulmonary metastases were discovered during the initial period after recurrence. According to Koga et al. [10], the incidence of pulmonary metastasis seen clinically was 7 (0.5%) in 1,314 gastric cancer resections. Among our patients we found such recurrence in 22 (0.7%) of the 3,076 curative gastrectomies for gastric cancer. This is consistent with the data of Koga et al. [10], and these findings show that the incidence of pulmonary metastasis from gastric cancer is very low at the clinical level. Furthermore, Yamauchi et al. [11] reported that the frequency of pulmonary metastasis appearing as a sole initial symptom was only 9 (0.3%) in 2,654 gastric cancer resections. However, nearly all of these pulmonary metastases accompanied lymphangitis carcinomatosa following an acute clinical course. Like these, resectable solitary pulmonary metastasis from gastric cancer in the absence of other organ metastasis is anticipated to be infrequent, but there is

presently no report concerning the frequency of such metastasis. The number in our series, 4 solitary pulmonary metastases (0.1%) in 3,076 curative resections for gastric cancer, is itself an indication of the frequency of solitary metastasis limited to the lung in patients with gastric cancer; therefore, encountering such cases in clinical settings is extremely rare.

Multiple malignancies are not rare. Warren and Gates [12] garnered multiple primary malignancies from their own series of 2,829 autopsies on patients with cancer, for an incidence of 6.8%. Therefore, the pathologist is often challenged with determining whether a tumor in the lung is primary or metastatic. Casey et al. [13] reviewed 1,416 patients with breast cancer. Forty-two (3%) of these patients had a solitary pulmonary nodule either at the time of presentation with their breast cancer or during the follow-up period. Further evaluation revealed that in only 43% of these patients the thoracic lesion represented metastasis, and in 52% they were primary lung tumors. Casey et al. [13] noted that most solitary pulmonary lesions in patients with breast cancer do not represent breast metastases.

Statistically, the incidence of a second primary lung

cancer in patients with gastric cancer has been reported to be 0.5%–1.7% in Japan [14,15]. These data show that by absolute numbers, second primary lung cancers in patients with gastric cancer far outnumber solitary lung metastases from gastric cancer we noted in this series. This may be reasonable when there are multiple pulmonary lesions in the patients with gastric cancer; the traditional reaction of most physicians has been that such a pulmonary lesion represents metastasis from the gastric cancer. However, the presence of a solitary pulmonary nodule can cause confusion with primary lung cancer in patients with gastric cancer. Diagnostically, special attention of the pathologist is needed to compare sections from the two organs to search for continuity of the lesion with the bronchial epithelium or attempts by the tumor to form ducts, and to use special staining techniques. Immunohistochemical study may be required for definitive differentiation. Finally, it may be difficult or impossible to differentiate a primary lung adenocarcinoma from a gastric metastasis in the diagnostic workup with the small amounts of specimen material obtained by trans-thoracic needle biopsy or bronchoscopic biopsy. In this series, the lung tumor in patient 2 was regarded as primary lung cancer preoperatively and the remaining patients underwent operations to confirm the diagnosis as pulmonary metastasis or primary lung cancer.

Hematogenous metastasis is closely related to invasion by malignant cells of the blood vessel in gastric cancer tissue. Gastric cancer cells in the blood vessel are disseminated to various organs through the portal vein. At this time, the liver becomes the first filter of cancerous cells, the lung acts as a second filter, and the bone as the third [16]. Therefore, metastases in the liver where malignant cells are intercepted may occasionally be curatively resected in selected patients [17], whereas metastasis to the lung without evidence of concomitant extrapulmonary metastases may be followed by passage through the liver and accompanied by systemic metastases at the time of thoracotomy as shown in our patients, most of whom developed multiple metastases in the lung, liver, bone, or brain within 1 year after pulmonary resection.

CONCLUSIONS

When a solitary pulmonary nodule appears in a patient with gastric cancer, either past or present, it is recommended that a preliminary staging workup proceed with

the assumption that the lesion represents a primary lung cancer. Therefore, if malignancy is proved or suspected, thoracotomy with appropriate resection is not contraindicated for those patients to make a differential diagnosis. However, when the obtained tissue reveals a pulmonary metastasis from gastric cancer, even if it is a solitary lesion limited to the lung, surgical treatment may not improve the prognosis.

REFERENCES

1. Goya T, Miyazawa N, Kondo H, et al.: Surgical resection of pulmonary metastases from colorectal cancer: 10-year follow-up. *Cancer* 1989;64:1418–1421.
2. Okumura S, Kondo H, Tsuboi M, et al.: Pulmonary resection for metastatic colorectal cancer: Experiences with 159. *J Thorac Cardiovasc Surg* 1996;112:967–974.
3. Fourquier P, Regnard JF, Rea S, et al.: Lung metastases of renal cell carcinoma: Results of surgical resection. *Eur J Cardio Thorac Surg* 1997;11:17–21.
4. UICC: TNM classification of malignant tumours, 4th ed. Berlin: Springer; 1992.
5. Bains MS, Ginsberg RJ, Jones WG, et al.: The clamshell incision: An improved approach to bilateral pulmonary and mediastinal tumor. *Ann Thorac Surg* 1994;58:30–33.
6. Thomford NR, Woolner LB, Clagett OT, et al.: The surgical treatment of metastatic tumors in the lung. *J Thorac Cardiovasc Surg* 1965;49:357–363.
7. Kawai A, Fukuma H, Beppu Y, et al.: Pulmonary resection for metastatic soft tissue sarcomas. *Clin Ortho* 1995;310:188–193.
8. Dupont JB Jr, Lee JR, Burton GR, et al.: Adenocarcinoma of the stomach: Review of 1,497 cases. *Cancer* 1978;41:941–947.
9. Ishii T, Ikegami N, Hosoda Y, et al.: The biological behaviour of gastric cancer. *J Path* 1981;134:97–115.
10. Koga S, Takebayashi M, Karibara N, et al.: Pathological characteristics of gastric cancer that develop hematogenous recurrence, with special reference to the site of recurrence. *J Surg Oncol* 1987;36:239–242.
11. Yamauchi M, Yamada E, Miyaishi S, et al.: Lung metastasis of gastric cancer. *Jpn J Cancer Clin* 1982;28:1243–1248.
12. Warren S, Gates O: Multiple primary malignant tumors: A survey of the literature and a statistical study. *Am J Cancer* 1932;16:1358–1414.
13. Casey JJ, Stempel BG, Scanlon EF, et al.: The solitary pulmonary nodule in the patient with breast cancer. *Surgery* 1984;96:801–805.
14. Kaibara N, Maeta M, Ikeguchi M: Patients with multiple primary gastric cancers tend to develop second primaries in organs other than the stomach. *Surg Today* 1993;23:186–188.
15. Ikeguchi M, Ohfuji S, Oka A, et al.: Synchronous and metachronous primary malignancies in organs other than the stomach in patients with early gastric cancer. *Hepato-Gastroenterology* 1995;42:672–676.
16. Kitaoka K, Suemasu K, Hirota E: Adhesive foci between cells and liver metastasis in cases of gastric cancer. *Jpn J Cancer Clin* 1972;18:534–537.
17. Ochiai T, Sasako M, Mizuno T, et al.: Hepatic resection for metastatic tumours from gastric cancer: Analysis of prognostic factors. *Br J Surg* 1994;81:1175–1178.